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NANOPARTICLES IN TUBERCULOSIS DIAGNOSIS, TREATMENT AND PREVENTION: A HOPE FOR FUTURE

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Scientific community believe that nanotechnology offers new ways to address residual scientific concerns for *Mycobacterium tuberculosis* (TB). Nanoparticle-based systems have significant prospective for diagnosis, treatment and prevention of tuberculosis (TB). Nanoparticles based tuberculosis diagnostic kits are under trial and have fascinating in sense that it is not required skilled hand and also have low cost. Another significant advancement of this technology is that the using of nano particles as drug carriers are has high stability and carrier capacity. The possibility of drug administration by oral and inhalation route make it more advantageous. The controlled drug release from the matrix, such properties of nanoparticles enable improvement of drug bioavailability and reduction of the dosing frequency, and may resolve the problem of non adherence to prescribed therapy. The development of aerosol vaccine is undergoing which could provide a great potential in prevention of tuberculosis infection. Keeping in mind the role of nanoparticles in these three aspects like diagnosis, treatment and prevention of tuberculosis, this article is the attempts to compile these aspects in hope for better advancements.

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1. Introduction

Tuberculosis (TB) in humans has been described since ancient times and its causative agent, *Mycobacterium tuberculosis* (MTB) is widely disseminated. The WHO estimates that approximately one-third of the global community is infected with *M. tuberculosis* [1]. In 2006, an estimated 9.2 million incident cases and approximately 1.7 million deaths due to TB occurred worldwide making it the worlds leading causes of mortality [2]. Despite mass *Mycobacterium bovis* BCG vaccination and the development of antitubercular drugs, tuberculosis still remains a major global public health problem.

The clinical management of tuberculosis and other mycobacterial diseases with anti-mycobacterial chemotherapy remains a difficult task. The classical treatment protocols are long-lasting; the drugs reach mycobacteria infected macrophages in low amounts and/or do not persist long enough to develop the desired anti mycobacterial effect; and the available agents induce severe toxic effects.

Nanotechnology has provided a huge improvement to pharmacology through the designing of drug delivery systems able to target phagocytic cells infected by intracellular pathogens, such as mycobacteria. The increased therapeutic index of anti-mycobacterial drugs; the reduction of dosing frequency; and the improvement of solubility of hydrophobic agents, allowing the administration of higher doses, have been demonstrated in experimental infections.

These advantages may lead to new therapeutic protocols that will improve patient compliance and, consequently, lead to a more successful control of mycobacterial infections. The

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Rising rates of tuberculosis and drug-resistant disease in developing countries have also amply illustrated the need for better diagnostic tools and effective vaccines. Because still we don't have a highly efficient method in relation to diagnose tuberculosis. This article reviews the relevant publications describing the future of nanoparticles in reference to diagnosis, treatment and prevention of *M. tuberculosis.*

2. Nanotechnology in diagnosis of tuberculosis

The diagnosis tools are required to meet the needs of the WHO's expansion of the Directly Observed Treatment Short-course, MDR and co-infection with HIV. In India, the country with the highest estimated number of TB cases, research is underway into the role nanotechnology can play in addressing such concerns. The Central Scientific Instruments Organization of India designed a nanotechnology-based TB diagnostic kit, which is currently in the clinical trials phase. This kit does not require skilled technicians for use and offers portability, efficiency, user-friendliness and availability for less than US$1. The research is also ongoing for an optical biosensor for rapid TB detection in the Medical Sciences division of the U.S. Department of Energy. Another group at RMIT University, in Australia, is conducting research into the application of novel tethered nanoparticles as low-cost, colour based assays for TB diagnosis [3].

3. Nanotechnology in treatment of tuberculosis

Treatments with improved sustained release profiles and bioavailability can increase compliance through reduced drug requirements and there in minimize MDR-TB. Chemotherapy of TB is complex due to the requirement of multi drug regimens that need to be administered over long periods. The Poor patient compliance is the single most common reason for chemotherapy failure in TB [4].

The micro-encapsulation of pharmaceutical substances in biodegradable polymers used in controlled drug delivery has seen as an emerging technology. Carrier or delivery systems such as liposomes and microspheres have been developed for the sustained delivery of anti-TB drugs and have found better chemotherapeutic efficacy when investigated in animal models (e.g. mice) [5].

The following are among the important technological advantages of nanoparticles as drug carriers: high stability (i.e., long shelf life); high carrier capacity (i.e., many drug molecules can be incorporated in the particle matrix); feasibility of incorporation of both hydrophilic and hydrophobic substances; and feasibility of variable routes of administration, including oral administration and inhalation. These carriers can also be designed to enable controlled (sustained) drug release from the matrix **[6]**. **Gelperina *et al.*** summarizes major data on nano-particulate formulations of the anti-TB drugs [6].

Table 1. Drug Release and Therapeutic Efficacy of the Nanoparticle-Based Formulations of the First-Line Antituberculous Drugs—Rifampin, Isoniazid, and Pyrazinamide

Delivery System	Animal Model	Administration Route	Duration of Drug Release (*d*)		Regimen Producing Sterilizing Effect in Lungs and Spleen	Reference
			Plasma	Organs		
PLG nanoparticles	Mice	Oral	6–9	9–11	5 doses every 10 d	7
	Mice	Subcutaneous	32	36	Single injection	8
	Guinea pigs	Aerosol	4–9	up to 10 d (each drug)	5 doses every 10 d	9
	Guinea pigs	Oral	4–9	up to 10 d (each drug)	5 doses every 10 d	9
Lectin-functionalized PLG nanoparticles	Guinea pigs	Oral	7–13	up to 15 d (each drug)	3 doses fortnightly	9
	Guinea pigs	Aerosol	6–14	up to 15 d (each drug)	3 doses fortnightly	9
Solid lipid nanoparticles	Guinea pigs	Aerosol	5	7	7 doses weekly	10

(Gelperina *et al.*, 2005)

(PLG = poly (lactide-co-glycolide). The drug-to-polymer ratio is 1:1 for each drug)

Indian research group from Postgraduate Institute of Medical Education and Research (India) has reported increased bioavailability and "undetectable bacterial counts in the lungs and spleens of *Mycobacterium tuberculosis*-infected mice" 21 days post-inoculation [11]. **Sharma *et al.* (2004)**, conducted a study to explore lectin-functionalized poly (lactide-co-glycolide) nanoparticles (PLG-NPs) as bio adhesive drug carriers against tuberculosis (TB), in order to reduce the drug dosage frequency of anti-tubercular drugs and thus improve patient compliance in TB chemotherapy. In this study they observed the presence of drugs in plasma for 6–7 days for rifampicin and 13–14 days for isoniazid and pyrazinamide after administration of lectin coated PLG-NPs through the oral/aerosol route. They also observed that upon administration of uncoated PLG-NPs (oral/aerosolized) rifampicin was detectable in plasma for 4–6 days, whereas isoniazid and pyrazinamide were detectable for 8–9 days. All three drugs were present in lungs, liver and spleen for 15 days. Obtaining these results they concluded that WGA-functionalized PLG-NPs could be potential drug carriers for antitubercular drugs through the oral as well as aerosol route for effective TB control [8].

Johnson *et al.*, (2005) evaluated the efficacy of nanoparticle-encapsulated anti-tuberculosis drugs administered every 10 days versus that of daily non encapsulated drugs against *Mycobacterium tuberculosis* aerosol infection in guinea pigs. In both cases the treatments significantly reduced the bacterial count. This finding suggested that the nanoparticle drug delivery system has potential in intermitted treatment of tuberculosis [12].

Nanotechnology in vaccination for tuberculosis

The aerosol vaccine- under development through collaboration between Harvard University and the international not-for-profit Medicine in Need (MEND) - could provide a low-cost, needle-free TB treatment that is highly stable at room temperature. While most new TB vaccines continue to call for needle injection, but this new vaccine could provide safer, more consistent protection by eliminating these injections and the need for refrigerated storage.

A successful result of aerosol delivery using nanoparticle technology offers a potentially new platform for immunization. Among guinea pigs vaccinated with the aerosol treatment and subsequently exposed to TB, less than 1 percent of lung and spleen tissue showed effects of the

disease. By contrast, in animals treated with the same dose of the traditional injected vaccine, some 5 percent of lung tissue and 10 percent of spleen tissue showed symptoms following TB exposure.

In the aerosol vaccine, particles form at micrometer and nanometer scales and in spherical and elongated shapes, a combination that appears to improve dispersal in the mouth. While commonly used with food, cosmetics, and pharmaceuticals, this spray drying of small and large molecules is seldom used for drying cellular material. The new technique enables TB vaccines, and potentially other bacterial and viral-based vaccines, to sidestep the traditional problems associated with keeping vaccines chilled. Furthermore, a nanotechnology-based vaccine adjuvant for TB was developed by the U.S firm, Biosante, in 2002 [3].

4. Conclusions

Scientific developments and increasing international attention have promoted our ability to work with and understand the nano scale. Nanotechnology provides a new focus for research through its aim to manufacture from the ‘bottom-up’ rather than from the ‘top down’. It also demands an unprecedented collaborative and integrated approach to science and technology. In an area such as tuberculosis, nanotechnology has the potential to empower a local response to challenges such as the diagnosis and treatment and prevention of this deadly disease and we can see its as a better approach to solve out the all problems.

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